UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/629,123	07/28/2003	David Pickar	26811-010 UTIL	5912

7590 04/12/2007

Ivor R. Elrifi
MINTZ, LEVIN, COHN, FERRIS, GLOVSKY AND POPEO P.C.
24th Floor
666 Third Avenue
New York, NY 10017

EXAMINER	
SOROUSH, LAYLA	
ART UNIT	**PAPER NUMBER**
1617	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/12/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/629,123	PICKAR ET AL.	
	Examiner	Art Unit	
	Layla Soroush	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,11-71 and 75* is/are pending in the application.

4a) Of the above claim(s) *11-14,24,29,32-34,50 and 54-62* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,15-23,25-28,30,31,35-49,51-53 and 63-71* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/15/05; 1/12/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The Office Action is in response to the Applicant's reply filed October 27, 2006 and February 6, 2007 to the restriction requirement made on July 27, 2006.

Applicant's election of without traverse Group I claims 1-6, 11-30, 31-34, 35-53, 54-71 and 75 and the species idazoxan as the a2-adrenergic receptor antagonist and olanzapine as the typical antipsychotic neuroleptic (in the reply filed on October 27, 2006) is acknowledged.

Applicant's election of the species schizophrenia as the condition or disease to be treated (in the reply filed on February 6, 2007) is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

The restriction requirement is deemed proper and made **FINAL**.

Claims 11-14, 24, 29, 32-34, 50, and 54-62 are withdrawn from further consideration pursuant to 37 C.F.R. 1.142(b), as being drawn to non-elected subject matter. Claim 75 is withdrawn as being dependent on a nonelected group of the restriction requirement. The claims corresponding to the elected subject matter are 1-6, 15-23, 25-28, 30-31, 35-49, 51-53, 63-67, and 68-71 are herein acted on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 22, 28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is unclear from the claim language what is meant by "reduced to approximately 50% of the normally recommended dosage." There are no metes and bounds to the claimed limitation.

Claims 68-71 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is unclear from the claim language what is meant by "the dosage balance between the atypical antipsychotic and alpha-2 antagonist" being "equivalent to a ratio of 900-1100mg equivalents of chlorpromazine and and an amount of an alpha2 antagonist that provides for about equal D2/alpha2 receptor saturation. The specification fails to define what "the dosage balance between the atypical antipsychotic and alpha-2 antagonist."

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-6, 15-21, 23, 25-27, 30-31, 35-49, 51-53, and 63-67 and are rejected under 35 U.S.C. 103(a) as being unpatentable over Pickar et al. (US Pat. No. 5,492,907) in view of Beasley, Jr. et al. (US Pat. No. 5,605,897).

Pickar et al. teaches a method for treating a serious psychotic mental illness such as schizophrenia, schizoaffective illnesses by administering to a patient in need thereof a (i) an alpha-2 adrenergic receptor antagonist such as idazoxan in 60 to 120 mg/day and (ii) a D2 dopamine receptor antagonist (col 6, claims 1-3). The reference further teaches "both the alpha-2 -adrenergic receptor antagonist and the antipsychotic neuroleptic can be administered in separate form. The two compounds can also be administered in a single pharmaceutical composition, in combination with known pharmaceutically acceptable carriers." The general teaching of treatment of patients, renders obvious the treatment any age group; therefore, the limitations of claims 51-53 are met.

Pickar et al. does not teach the specific D2 dopamine receptor antagonist as claimed.

Beasley, Jr. et al. teaches olanzapine an antagonist of dopamine at D-1 and D-2 receptors, and in addition has anti-muscarinic anticholinergic properties and antagonist activity at 5HT-2 receptor sites. It also has antagonist activity at noradrenergic α-receptors. The reference teaches the treatment of schizophrenic patients with 2-methyl-4-(4-methyl-1-piperazinyl)-10H-thieno[2,3-b][1,5]benzodiazepine (olanzapine) (col 7, lines 23-27)." Further, preferably, olanzapine is used in the treatment of various schizophrenic disorders (col 6, lines 32-64). The limitation of claim 23 wherein the d2

dopamine and 5HT-2 serotonin antagonist comprises an in vivo D2 occupancy of 50%, is a property of the compound. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. Additionally, the limitations of claims 35, 36, wherein the antipsychotic effects at D2 receptor occupancy levels of less than or equal to 60%; or 50% and the limitations of claims 63-67, wherein the receptor affinity ratios for D2 or alpha2 ranges from 0.8-4.5, 0.85-3.9, 0.95-1.05, 0.95-1.00, and 1.0 is a property of the compound. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present.

Claims 37, limitation of measuring the D2 occupancy levels by PET or SPECT does not further limit the claimed invention, therefore the limitation receives no patentable weight in a method of treatment claim.

It would have been obvious to one of ordinary skill in the art to incorporate the D2 dopamine receptor antagonist of Beasley Jr. et al. into the invention of Pickar et al. because Pickar teaches the use of a D2 dopamine receptor antagonist in a pharmaceutical formulation used to treat serious psychotic mental illnesses and Beasley Jr. et al. teaches the D2 dopamine receptor antagonist, olanzapine, used in treating disorders of the central nervous system such as Schizophreniform Disorder. The motivation to use olanzapine as the D2 dopamine receptor antagonist is because Beasley Jr. et al. teaches “overall, therefore, in clinical situations, olanzapine shows

marked superiority, and a better side effects profile than prior known antipsychotic agents, and has a highly advantageous activity level (col 2, lines 49-55)." Therefore, a skilled artisan would have reasonable expectation of successfully producing a pharmaceutical composition with the same efficacy and results.

Additionally, the limitation to enantiomers recited in claims 44-49 is rendered obvious over the racemic mixture. A person having ordinary skill in the art would have known that the racemic mixture of the prior art may be separate (+) and (-) would have been motivated to do so with reasonable expectation of achieving enantiomers of (+) and (-) with beneficial results. In the absence of showing the criticality, the mole ratios of the enantiomers are deemed to be manipulatable parameters practiced by an artisan to obtain the best possible pharmaceutical results.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 2, 3, 5, and 6 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3, and 5 of U.S. Patent No. 5492907 in view of Beasley, Jr. et al. (US Pat. No. 5,605,897).

Pickar et al. teaches a method for treating a serious psychotic mental illness such as schizophrenia, schizoaffective illnesses by administering to a patient in need thereof a (i) an alpha-2 adrenergic receptor antagonist such as idazoxan in 60 to 120 mg/day and (ii) a D2 dopamine receptor antagonist (col 6, claims 1-3). The reference further teaches "both the alpha-2 -adrenergic receptor antagonist and the antipsychotic neuroleptic can be administered in separate form.

Pickar et al. does not teach the specific D2 dopamine receptor antagonist as claimed.

Beasley, Jr. et al. teaches olanzapine an antagonist of dopamine at D-1 and D-2 receptors, and in addition has anti-muscarinic anticholinergic properties and antagonist activity at 5HT-2 receptor sites. It also has antagonist activity at noradrenergic α-receptors. The reference teaches the treatment of schizophrenic patients with 2-methyl-4-(4-methyl-1-piperazinyl)-10H-thieno[2,3-b][1,5]benzodiazepine (olanzapine) (col 7, lines 23-27)." Further, preferably, olanzapine is used in the treatment of various schizophrenic disorders (col 6, lines 32-64).

It would have been obvious to one of ordinary skill in the art to incorporate the D2 dopamine receptor antagonist of Beasley Jr. et al. into the invention of Pickar et al. because Pickar teaches the use of a D2 dopamine receptor antagonist in a

pharmaceutical formulation used to treat serious psychotic mental illnesses and Beasley Jr. et al. teaches the D2 dopamine receptor antagonist, olanzapine, used in treating disorders of the central nervous system such as Schizophreniform Disorder. The motivation to use olanzapine as the D2 dopamine receptor antagonist is because Beasley Jr. et al. teaches "overall, therefore, in clinical situations, olanzapine shows marked superiority, and a better side effects profile than prior known antipsychotic agents, and has a highly advantageous activity level (col 2, lines 49-55)." Therefore, a skilled artisan would have reasonable expectation of successfully producing a pharmaceutical composition with the same efficacy and results.

Claims 1, 2, 3, 5, and 6 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4, 6 and 7 of U.S. Patent No. 5663167 in view of Beasley, Jr. et al. (US Pat. No. 5,605,897)..

Pickar et al. teaches a method for treating a serious psychotic mental illness such as schizophrenia, schizoaffective illnesses by administering to a patient in need thereof a (i) an alpha-2 adrenergic receptor antagonist such as idazoxan in 60 to 120 mg/day and (ii) a D2 dopamine receptor antagonist .

Pickar et al. (5663167) does not teach the specific D2 dopamine receptor antagonist as claimed.

Beasley, Jr. et al. teaches olanzapine an antagonist of dopamine at D-1 and D-2 receptors, and in addition has anti-muscarinic anticholinergic properties and antagonist activity at 5HT-2 receptor sites. It also has antagonist activity at noradrenergic α-

receptors. The reference teaches the treatment of schizophrenic patients with 2-methyl-4-(4-methyl-1-piperazinyl)-10H-thieno[2,3-b][1,5]benzodiazepine (olanzapine) (col 7, lines 23-27)." Further, preferably, olanzapine is used in the treatment of various schizophrenic disorders (col 6, lines 32-64).

It would have been obvious to one of ordinary skill in the art to incorporate the D2 dopamine receptor antagonist of Beasley Jr. et al. into the invention of Pickar et al. because Pickar teaches the use of a D2 dopamine receptor antagonist in a pharmaceutical formulation used to treat serious psychotic mental illnesses and Beasley Jr. et al. teaches the D2 dopamine receptor antagonist, olanzapine, used in treating disorders of the central nervous system such as Schizophreniform Disorder. The motivation to use olanzapine as the D2 dopamine receptor antagonist is because Beasley Jr. et al. teaches "overall, therefore, in clinical situations, olanzapine shows marked superiority, and a better side effects profile than prior known antipsychotic agents, and has a highly advantageous activity level (col 2, lines 49-55)." Therefore, a skilled artisan would have reasonable expectation of successfully producing a pharmaceutical composition with the same efficacy and results.

Conclusion

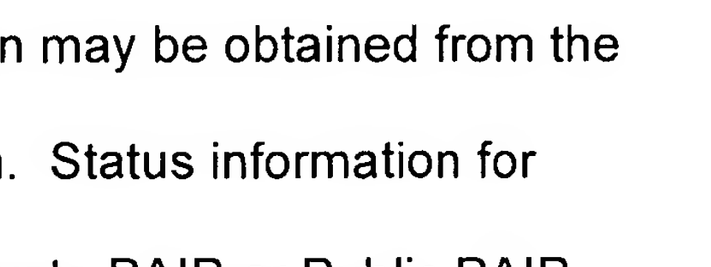
No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Layla Soroush whose telephone number is (571)272-

5008. The examiner can normally be reached on Monday through Friday from 8:30 a.m. to 5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER